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10/027,000	12/18/2001	Nigel Dunn-Coleman	GC696	9426

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EXAMINER

RAO, MANJUNATH N

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 06/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/027,000

Applicant(s)

DUNN-COLEMAN ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 18,21,25 and 27-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17,19,20,22-24 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Claims 1-36 are now currently pending in this application. Claims 1-17, 19-20, 22-24 and 26 are now under consideration. Claims 18, 21, 25, 27-36 remain withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicant's election of group I, claims 1-17, 19-20, 22-24 and 26 in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Objections

Claim 2 is objected to because of the following informalities: Claim 2 recites duplicate limitations. Duplicate parts are part (c); part (e) and part (d); part(f). Appropriate correction is required.

Applicants do not recite biological names in italics in which ever claims they occur. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6, 7, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 6, 7 recite the phrase "derived from". The metes and bounds of this phrase in claims is not clear to the Examiner. Literally, while the term "derived" means "to isolate from or obtain from a source", the above term could also mean "to arrive at by reasoning i.e., to deduce or infer" or also mean "to produce or obtain from another substance". Therefore, it is not clear to the Examiner either from the specification or from the claims as to what applicants mean by the above phrase. It is not clear to the Examiner whether the "derived from a fungal source or derived from *Trichoderma*" encompasses only fungi or *Trichoderma* as in "isolated from a fungal source or isolated from *Trichoderma*" or whether it encompasses recombinants, variants and mutants obtained from any source and labeled as "derived from a fungal source or derived from *Trichoderma*". As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean, that a "derived from " encompasses all or any source. Examiner has given the same interpretation while considering the claims for all other rejections.

Claims 8-9, 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 8 and 9 recite the phrases "including a polynucleotide" and "including the

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expression construct". The meaning of the above phrase in the context of the above claim is not clear to the Examiner. It appears that applicant intended to recite "comprising a polynucleotide", and "comprising the expression construct" respectively. If this is so amending the claim accordingly would overcome this rejection.

Claim 8 and claims 9 and 11 dependent therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 recites the phrase "an expression construct...having at least 85% sequence identity to the amino acid sequence in figure 2, (SEQ ID NO:2)" and "being capable of ...nucleotide sequence disclosed in figure 2..." and "being complementary to a nucleotide sequence having at least 85% sequence identity to the amino acid sequence presented in figure 2 (SEQ ID NO:2)". Figure 2 represents the amino acid sequence and not nucleic acid sequence. Applicants are directly comparing the claimed nucleic acid with an amino acid sequence which are structurally and functionally different from each other. Correction is required.

Claim 23 and claim 24 dependent therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 23 recites the phrase "decreases or inhibits". The metes and bounds of the above phrase is not clear to the Examiner, specifically the term, "decreases" rendering the claim indefinite.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, 19-20, 22, 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide isolated from *T.reesei*, with SEQ ID NO:1, 3 encoding a polypeptide with SEQ ID NO:2 having beta-glucosidase activity and a method of making said beta-glucosidase by transforming a host cell with an expression vector comprising the polynucleotide with SEQ ID NO:3 followed by cultivating the host cells and recovering the expressed beta-glucosidase, a recombinant host cell in which the polynucleotide with SEQ ID NO:3 has been inactivated such that it does not express a functional beta-glucosidase, does not reasonably provide enablement for a polynucleotide isolated from any all sources, or a polynucleotide that has 85%, 90%, or 95% identity to the polynucleotide encoding the polypeptide with SEQ ID NO:2 or any polynucleotide that hybridizes under high stringency conditions to SEQ ID NO:3 or polynucleotides that hybridize under intermediate to high stringency conditions to the polynucleotide encoding polypeptide with SEQ ID NO:2, or encoding a polypeptide having beta-glucosidase activity and a method of making said beta-glucosidase by transforming a host cell with an expression vector comprising the said polynucleotide followed by cultivating the host cells and recovering the expressed beta-glucosidase or a recombinant host cell in which any polynucleotide encoding any bgl4 β -glucosidase has been inactivated such that it does not express a functional beta-glucosidase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

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Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-17, 19-20, 22, 26 are so broad as to encompass any polynucleotide from any source encoding a beta-glucosidase, vectors host cells and methods of expressing said beta-glucosidase. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a given polynucleotide, determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single beta-glucosidase obtained from *T.reesei*. It would require undue experimentation of the skilled artisan to identify and make and use all the claimed polynucleotides. The specification is limited to teaching use of SEQ ID NO: 1 or 3 as a polynucleotide encoding the polypeptide with SEQ ID NO:2. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art

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in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polynucleotides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide with 85%, 90%, or 95% identity to the polynucleotide encoding the polypeptide with SEQ ID NO:2 or any polynucleotide that hybridizes under high stringency conditions to SEQ ID NO:3 or polynucleotides that hybridize under intermediate to high stringency conditions to the polynucleotide encoding polypeptide with SEQ ID NO:2 because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without effecting its activity of encoding a functional beta-glucosidase; (B) the general tolerance of said polynucleotide sequence to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide in the polynucleotide with an expectation of obtaining the desired biological

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function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides with an enormous number of modifications of SEQ ID NOS: 3. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1, 6-7, 19-20 22 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules encoding beta-glucosidase and a method of producing beta-glucosidase using DNA molecules encoding beta-glucosidase.

The specification does not contain any disclosure of the structure of all DNA sequences that are encompassed by the claims. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of having many different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot

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reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6-7, 19-20, 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Takashima et al.(J. Biochem., Vol. 125:728-736, 1999). This rejection is based upon the public availability of a printed publication. Claims 1, 6-7, 19-20, 26 of the instant application are drawn to an isolated polynucleotide derived from a fungal source encoding an beta-glucosidase (claim 1), wherein said polynucleotide is isolated from a *Trichoderma* source (claims 6-7), a method of producing said beta-glucosidase using the transformed host cells (claims 19-20), a method of expressing a heterologous polypeptide having beta-glucosidase activity in an *Aspergillus* species by transforming a *Aspergillus* host cell with an expression vector comprising a polynucleotide encoding a signal sequence linked to a polynucleotide encoding a heterologous beta-glucosidase encoding a chimeric polypeptide followed by cultivating said host cell such that the chimeric polypeptide is produced. Takashima et al. disclose a polynucleotide, encoding an beta-glucosidase, isolated from a *Trichoderma* sp., a method of producing said beta-glucosidase

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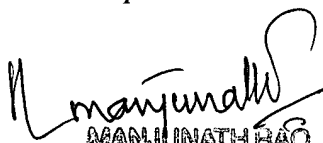
using the transformed host cells, a method of expressing a heterologous polypeptide having beta-glucosidase activity in an *Aspergillus* species (see page 730, column 2) by transforming a *Aspergillus* host cell with an expression vector comprising a polynucleotide encoding a signal sequence linked to a polynucleotide encoding a heterologous beta-glucosidase encoding a chimeric polypeptide followed by cultivating said host cell such that the chimeric polypeptide is produced. Therefore, Takashima et al. anticipate claims 1, 6-7, 19-20, 26 as written.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao
June 23, 2003